A JOURNEY THROUGH THE OXADIAZOLE-BASED COMPOUNDS: FROM SYNTHESIS TO APPLICATIONS

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Abstract. *2,5-Disubstituted-1,3,4-oxadiazoles emerged as compounds with great utility in the field of medicinal and materials chemistry. Research in the chemistry of the oxadiazole derivatives has developed with the evolution of each application area and the need of target molecules with specific properties. We describe herein a survey of literature over the recent progress in synthesis of 1,3,4-oxadiazoles, their incorporation in bioactive molecules or functional scaffolds for preparation of materials.*

Contents

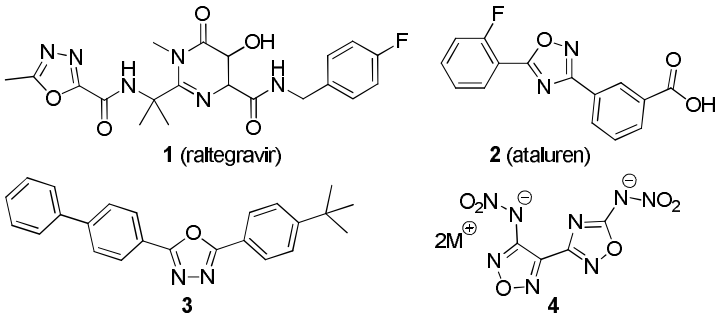
1. Introduction
2. Synthesis of the 1,3,4-oxadiazole compounds
3. Applications of the 1,3,4-oxadiazole derivatives
  3.1. Medicinal chemistry
  3.2. Materials chemistry
    3.2.1. Organic-Light Emitting Diodes
    3.2.2. Liquid crystals
    3.2.3. Sensors for cations and anions, metal-ion complexes and coordination polymers
    3.2.4. Others
4. Conclusions
Acknowledgments
References

1. Introduction

Oxadiazoles constitute a class of heterocyclic organic compounds that attracted attention due to their multiple applications in medicinal and materials chemistry. Except the 1,2,3-oxadiazole, which is unstable,[1] the isomeric oxadiazole-based (1,2,4-, 1,2,5-, 1,3,4-) moieties can be encountered in molecules acting as drugs on the market or in final clinical trials (Scheme 1, *i.e.* compound **1** named *raltegravir*[2] is an antiretroviral drug against HIV, while compound **2**, named *ataluren* is a good candidate for treatment of cystic fibrosis[3]), suitable materials [Scheme 1, *i.e.* compound **3**[4], for construction of Organic Light Emitting Diodes (OLEDs)][5] or highly energetic materials[6] (Scheme 1, *i.e.* compounds of type **4** in the form of salts), just to name a few applications.

The 1,3,4-oxadiazole-derivatives are the most stable among the oxadiazole isomers[7] and have attracted most in the form of small-molecule or polymers, mainly for construction of OLEDs[5] and synthesis and investigation of biologically complex active molecules.[8] There are numerous other applications (*vide infra*)

that use some structural particularities and, hence, the appropriate properties of these heterocyclic compounds. All these prompted research of convenient synthetic procedures to make available complex molecules designed to display certain properties. Thus, the synthetic chemistry of the 1,3,4-oxadiazole heterocycles developed simultaneously with the particular evolution of each area that used these type of molecules.



Scheme 1

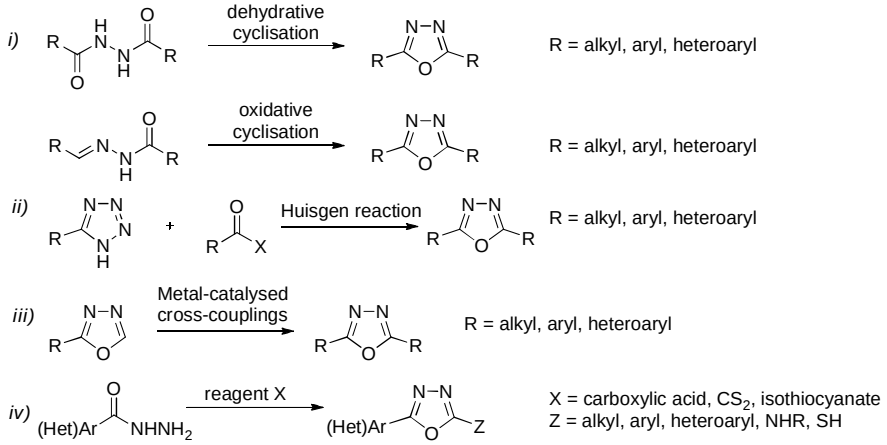
We describe herein the main synthetic approaches of the 1,3,4-oxadiazoles and congeners highlighting the structures that found utility in medicinal and biological chemistry as well as in materials sciences as molecules mainly acting as liquid crystals, ligands for metal-ions or displaying electron-transporting and hole blocking behaviours in OLEDs. The literature covering the 1,3,4-oxadiazole compounds is very vast and an exhaustive description of all their synthetic methods and applications exceeds the limits imposed for such a review. We will concentrate, thus, on the 2,5-diaryl-1,3,4-oxadiazoles and present the recent achievements in their synthesis and applications.

2. Synthesis of the 1,3,4-oxadiazole compounds

The synthetic approaches of the 2,5-disubstituted-1,3,4-oxadiazoles (Scheme 2) may involve: *i)* ring closure under dehydrative or oxidative conditions of acyclic precursors containing the required atoms in appropriate positions (*N*,*N'*-diacylhydrazines and *N*-acylhydrazones), leading to oxadiazole bearing a wide variety of 2- and/or 5-substituents; *ii)* Huisgen reactions of tetrazoles and acid chlorides; *iii)* reactions of 2-substituted-1,3,4-oxadiazoles, usually under transition metal catalysis; *iv)* one pot procedures involving compounds bearing nitrogen atoms (*i.e.* hydrazides) and another reagent that constitutes the 5-substituent source (*i.e.* carboxylic acid, CS_2 as sulfur source for synthesis of 1,3,4-oxadiazole-2-thiones, isothiocyanates for synthesis of amino derivatives etc.).

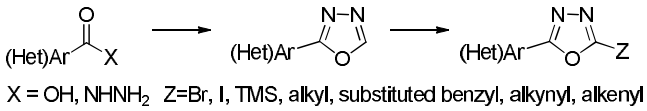
The alkyl-substituted-1,3,4-oxadiazoles are less encountered compared to their (het)aryl counterparts. Therefore, we will refer mainly to synthesis of the (het)aryl containing compounds and clearly specify when efficient procedures were reported for the preparation of the alkyl derivatives. 2-Het(aryl)-1,3,4-oxadiazoles may be readily available from reaction of the hydrazides (Scheme 3) with orthoesters,[9] styrene/phenylacetylene,[10] methylketones[11] but also starting from the carboxylic acids (Scheme 3) in reaction with (*N*-isocyanimino)triphenylphosphorane.[12] The convenient synthesis of these compounds

recently made them suitable reagents for further functionalization through the C-H bond by use of metal-catalysed cross-coupling reactions (Scheme 3).



Scheme 2

Thus, oxadiazoles substituted with alkynyl, alkenyl and benzyl were reported to have been synthesized, under palladium, nickel or copper catalysis, using a variety of alkynylating compounds (*i.e.* alkynes,[13] copper acetylides,[14] bromoalkynes[15] or *gem*-dibromoalkenes[16]), *β*-halostyrenes[17] and *N*-tosyl hydrazones[18] or benzyl carbonate,[19] respectively. The C-H bond in the oxadiazole structure is susceptible to substitution with halogen atoms (bromine[20] and iodine[21]) or trimethylsilyl group[22] that are also known to undergo cross-coupling reactions.[20,22b]

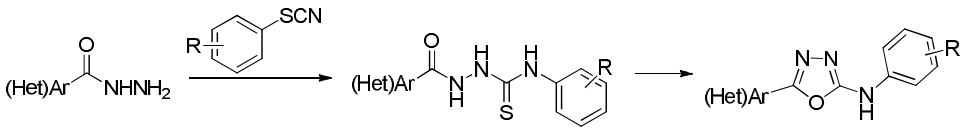


Scheme 3

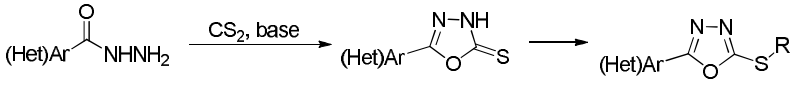
Arylation of 2-substituted-1,3,4-oxadiazoles using various iodobenzene derivatives,[23] boronic acids,[24] polyfluoroarenes[25] in presence of transition metal-catalysts constitutes other preparation methods that have been recently developed.

2-Amino-5-(het)aryl-1,3,4-oxadiazoles (Scheme 4) may be prepared from isothiocyanates and hydrazides or preformed acylthiosemicarbazides, by cyclisation with mild reagents such as carbodiimides,[26] 1,3-dibromo-5,5-dimethylhydantoin/KI,[27] tosyl chloride/pyridine,[28] uronium coupling reagents {*i.e.* TBTU [(O-(Benzotriazol-1-yl)-*N,N,N',N'*-tetramethyluronium tetrafluoro borate)]}.[29]

The sulfur-containing-1,3,4-oxadiazoles (Scheme 5) may be conveniently synthesized starting from the hydrazides using CS_2 as sulfur source,[30] leading to thiones which can subsequently be converted into methyl,[31] benzyl[32] or phenyl[33] thioethers.



Scheme 4



Scheme 5

Among the oxadiazole-containing compounds, the 2,5-diaryl-1,3,4-oxadiazoles have attracted most, and numerous synthetic procedures have been reported and reviewed.[8, 34] The most encountered precursors of the heterocyclic core are *N,N′*-diacylhydrazines, *N*-acylhydrazones or tetrazoles (Scheme 2), which furnish under variable conditions the target products.

For instance, the dehydrative cyclisation of the *N,N′*-diacylhydrazines has been reported to occur under the action of $POCl_3$,[35] $SOCl_2$,[36] zirconium(IV) chloride,[37] Tf_2O[38] or $[Et_2NSF_2]BF_4$,[39] while the oxidative cyclisation of the *N*-acylhydrazone can be usually performed using milder reaction conditions by use of cerium ammonium nitrate (CAN),[40] lead(IV) tetracetate,[41] acetic anhydride,[42] $Cu(OTf)_2$,[43] hypervalent iodine reagents[44] such as phenyliodine(III) diacetate (PIDA),[45] bis(trifluoroacetoxy)iodobenzene (PIFA)[46] or Dess-Martin reagent[47] and, more recently, molecular iodine.[48] The harsh conditions required by the dehydrative cyclisation are the major drawbacks that led to increase in the number of the oxidative cyclisation reagents. In addition, the *N*-acylhydrazones constitute more versatile precursors to furnish non-symmetrical oxadiazoles derivatives useful for various applications.[49]

Moreover, in an effort to simplify the preparation of the heterocyclic compounds, one pot procedures have been developed. Selected examples include reaction of carboxylic acids and hydrazides,[50] aryl tetrazoles and aldehydes[51] or iodobenzene,[52] aryliodides and hydrazides,[53] *N′*-(arylmethyl)hydrazides or 1-(arylmethyl)-2-(arylmethylene)hydrazines[54] or aldazines[55] with hypervalent iodine reagents.

The Huisgen reactions between tetrazoles and acid chlorides[56] have also been frequently reported for the synthesis of 2,5-diaryl-1,3,4-oxadiazoles. A recent report shows the action of triflic anhydride over tetrazole to yield trifluoromethyl-substituted-bis-oxadiazoles.[57]

Summarizing, the synthetic methodology of the oxadiazole congeners has been extensively investigated and a wide variety of simple and efficient procedures are available for their preparation, according to the structural demands of the applications that are further presented.

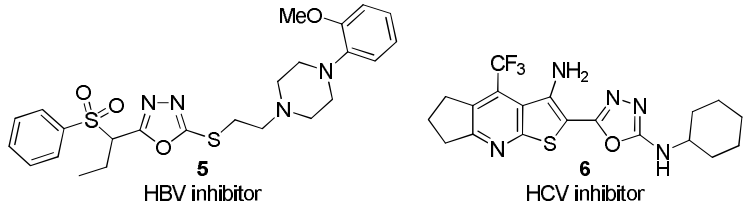
3. Applications of the 1,3,4-oxadiazole derivatives

3.1. Medicinal chemistry

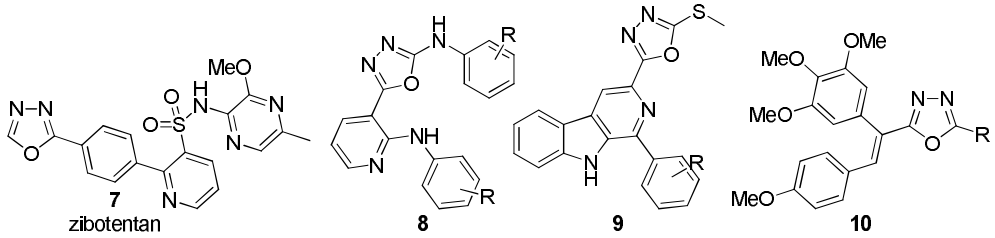
A plethora of literature is currently available for the use of 1,3,4-oxadiazole scaffold embedded in potentially active biological molecules.[8] Apart from the HIV antiviral *raltegravir*[2] **1** on the market (Scheme 1), compound **5** (Scheme 6) was synthesized and investigated as a hepatitis B virus (HBV) inhibitor[58] yielding an EC_{50} value of 1.63 μmol/L. Very recently,[59] structure **6** (Scheme 6) was found to inhibit hepatitis

C virus (HCV) GT-1b replicon with EC_{50}=0.039 nM, as a result of a detailed QSAR study which carefully optimised the substituents around the oxadiazole heterocyclic core.

Molecules able to act as anticancer agents have been investigated to a greater extent and a comprehensive review concerning this matter has been recently made available.[8a] The most prominent molecule is zibotentan[60] **7** (Scheme 7), which is currently in an advanced phase of the clinical trials. Various amino and thioorganic derivatives of the oxadiazoles are among the most encountered types of compounds that were thoroughly screened and showed promising *in vitro* activity, in micromolar to nanomolar range, for inhibition of the cancer cell lines. Examples of such compounds are numerous and we selected compounds **8**[61] and **9**[62] (Scheme 7) for demonstration purposes. Moreover, compounds of type **10**[63] substituted with various (het)aromatic moieties were screened as *Tubulin Polymerization* inhibitors. Among them, the 3,4,5-trimethoxyphenyl derivative was found lead compound with IC_{50} values down to 0.118 μM.



Scheme 6

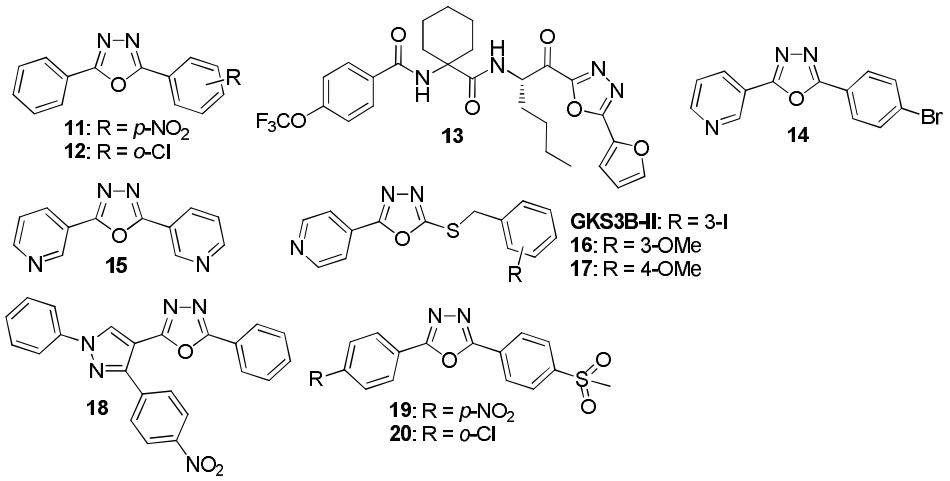


Scheme 7

Efficient inhibitors for various enzymes of interest based on the 1,3,4-oxadiazole scaffold have also been reported. For example, 2,5-diaryl-1,3,4-oxadiazoles of type **11** and **12** (Scheme 8) have been recently found to perform as competitive inhibitors against cathepsins B, L and H, respectively, with inhibition constants in the range 10^{-7}-10^{-9} M.[64] Further, compound **13** was proved to selectively inhibit cathepsin K, [65] by modifying the binding moieties around the heterocyclic core until the inhibition was achieved in the submolar range. Compound **14** was assayed to display an IC_{50} of 2.18 μM against tyrosinase[66] and compound **15**, bearing symmetrical 3-pyridyl moieties displayed an IC_{50} of 37 μM against thymidine phosphorylase.[67]

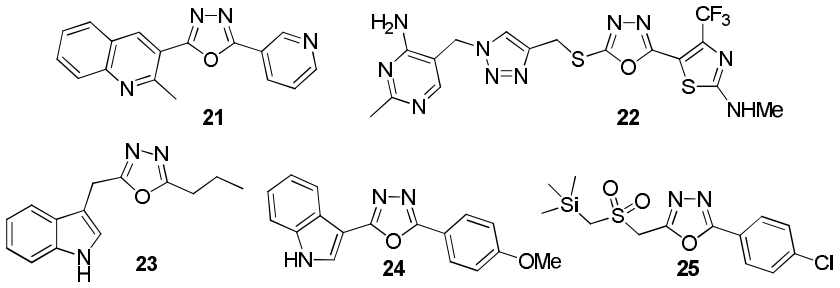
Moreover, starting from the commercially available GKS3B-II, known as efficient glycogen synthase kinase 3β inhibitor,[68] structures **16** and **17** (Scheme 8) were found to significantly reduce the level of superoxide dismutase (SOD1) expression up to 47–50% using a concentration of 10 μM.[69] The oxadiazole based compounds such as **18**,[70] **19** and **20**[71] (Scheme 8) were also found to perform well (IC_{50} in the

micromolar range) in assays against cyclooxygenase-2 enzyme (COX-2), known to be responsible in inflammation processes. Other studies worth mentioning involving the oxadiazole core were based on their amide isoster profile and included interaction with fatty acid amide hydrolase[72] or investigation of their lipophilicity[73] and the consequences over the biological effects.



Scheme 8

Along the years, the 1,3,4-oxadiazole derivatives have been widely tested and reported to have a good behaviour as antimicrobial agents and antifungal agents, having a wide range of substituents on the heterocyclic core and these have been reviewed in detail.[8b] Recent reports pointed out new structures efficient in the fight with bacteria that produces tuberculosis (compound **21** in Scheme 9)[74] or able to inhibit pyruvate dehydrogenase complex E1 in *E. coli* (IC_{50} 0.97μM) or cyanobacteria (EC_{50}=0.83 μM), such as compound **22** (Scheme 9). Indole-based 1,3,4-oxadiazoles like **23** and **24** (Scheme 9) are examples of compounds assayed for their antifungal properties,[75] while sila-substituted 1,3,4-oxadiazoles[76] of type **25** were screened for the antiallergic activity both *in vitro* and *in vivo*, yielding good results in reference to diphenylhydramine, an anti-histamine drug.



Scheme 9

Thus, as one can see, the pharmacological profile of the oxadiazole containing compounds has been thoroughly screened, proved to be very vast and molecules with simple or more complicated structures were designed, synthesized and assayed. Optimisation of the structural particularities are continuously performed in order to ensure a perfect match with the biological targets and, consequently, we expect a further development of the oxadiazole research area.

3.2. Materials chemistry

The increasing interest in preparation of various organic materials combined with good thermal and luminescent behaviour as well as the electron mobility ability of the 1,3,4-oxadiazole core made these heterocyclic derivatives good candidates for applications in construction of the optoelectronic devices as well as chemosensors for various metal-ions, construction of coordination polymers or liquid crystals. We will further describe examples and the latest achievements in these fields of the 1,3,4-oxadiazole compounds.

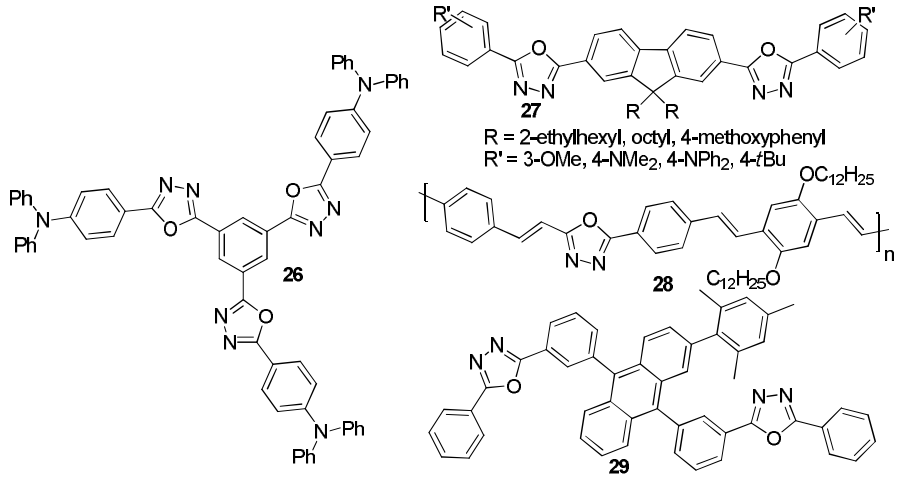
3.2.1. Organic-Light Emitting Diodes

The light emission in organic-light emitting diodes (OLEDs) can be achieved through use of conventional fluorescent, phosphorescent or thermally-activated delayed fluorescent (TDAF) based materials.[77] The emission of light in the fluorescent materials is due to the relaxation of the electrically excited singlet molecules and suffer from a low internal quantum efficiency of about 25% that is the statistically percentage of the singlet excitons. This limitation was overcome by development of phosphorescent materials that are able to harvest the triplet excitons (75%), thus allowing achievement of a higher internal quantum efficiency (100%, due to the mixed effect of the singlet and triplet excitons). This can be accomplished by use of heavy metal complexes of Ir(III), Os(II) or Pt(II) as emissive materials from the triplet state at room temperature, which, nonetheless, make the devices disadvantageous, due to the high cost of the metals. Discovery of TADF based materials is a recent breakthrough[78] which facilitates the reverse intersystem crossing of the triplet excitons to singlet excitons by heating, providing thus the harvesting of both excitons, without use of a metal. The improvement of the OLEDs efficiency occurred concomitantly with the evolution of the technological approaches for their construction, either as single or multi layered architectures,[79] which is based on a certain type of small-molecule or polymeric materials (for any of the hole injection, hole transporting, electron injection, electron transporting, emissive layers etc.) as well as on more complex structures that contain both electron-donor and acceptor moieties (also known as ambipolar molecules or donor-acceptor molecules). In addition, the vacuum deposition techniques are slowly being replaced by recent solution processed procedures, which benefit from a reduced cost for fabrication.[80]

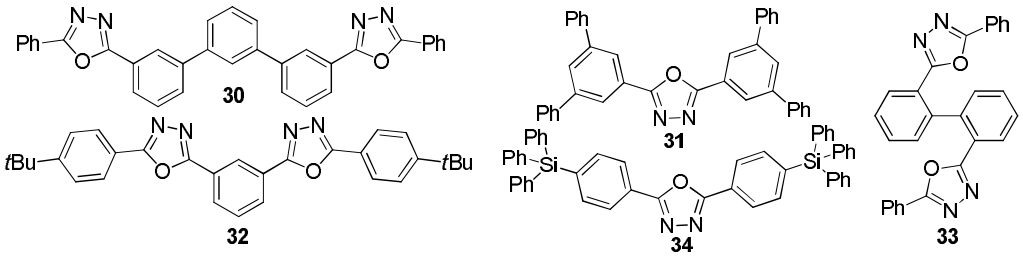
Since report of the first oxadiazole[4] compound (**3**, Scheme 1) acting as electron-transporting material for OLEDs, there was an increasing interest[5] to find more and more new such molecules containing this heterocyclic core providing better thermal, luminescent, electron transporting or hole blocking abilities that could play the role and meet the requirements of the above mentioned features to construct efficient optoelectronic devices.

For example, compound **26** (Scheme 10) was among the first small-molecules bearing more than one 1,3,4-oxadiazole unit to be considered in studies for construction of fluorescent devices at a time when these studies were incipient.[81] Compounds of type **27** were similar early examples of fluorescent molecules that yielded modest results, but had contributed to the development of the field.[82] Polymers[83] such as **28** (Scheme 10), as well as copolyfluorene polymers[84] containing variable amounts of oxadiazole, anthracene or anthracene/carbazole units were also synthesized and tested for their electroluminescent behaviour to yield blue light electronic devices. Recently, molecules with bulky or sterically hindered substituents (compound **29**, Scheme 10) were found to improve the blue colour of the assayed electroluminescent devices.[85]

Small molecules **30**-**34** depicted in Scheme 11 are several examples of derivatives that were designed, synthesized and investigated for applications as electron transporting molecules for phosphorescent devices. Compounds such as **30** and **31** were used for preparation of red, green and blue phosphorescent devices with external quantum efficiencies higher than 25%, as well as with good current and power efficiencies.[86] Similarly, compound **32** was reported to properly behave in construction of highly efficient monochromatic (blue, red and yellow) and white hybrid organic-inorganic phosphorescent LEDs, with high maximum external quantum efficiencies for the monochromatic devices as well as good luminance and power efficiencies for the white devices.[87]



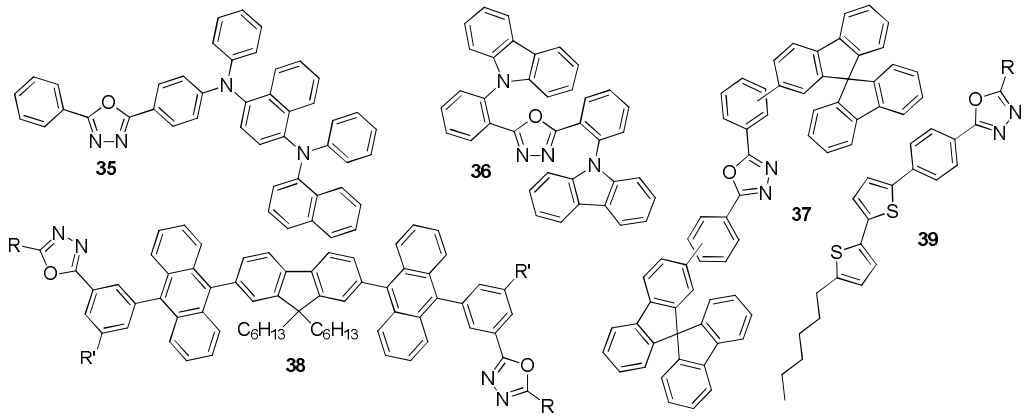
Scheme 10



Scheme 11

The highly twisted **33** (Scheme 11) was also found to perform well as electron transport host for the $Ir(ppy)_3$ emitter in phosphorescent OLEDs, due to good spectral matching with the absorption spectra of the iridium complex.[88] Silane-based-oxadiazoles **34** have also been recently developed as efficient materials for phosphorescent OLEDs with very good thermal properties.[89]

Bipolar small molecules have increasingly attracted due to the advantages brought by the presence of electron donor and acceptor units, and consequently, balanced electrons and holes fluxes that provide a greater probability of charge recombination and high triplet energies which are required for electroluminescence applications.[90] Thus, donor-acceptor molecules (Scheme 12) bearing an oxadiazole moiety as electron acceptor and various triarylamine-[91] (compound **35**), carbazole-[92] (compound **36**), spirobifluorene-,[93] (compounds of type **37**) anthracene-/fluorene-[94] (compounds of type **38**), or bithiophene-[95] (compound **39**) derived subunits, as electron donor units were embedded in the same skeleton and yielded good results for construction of a wide range of phosphorescent OLEDs.



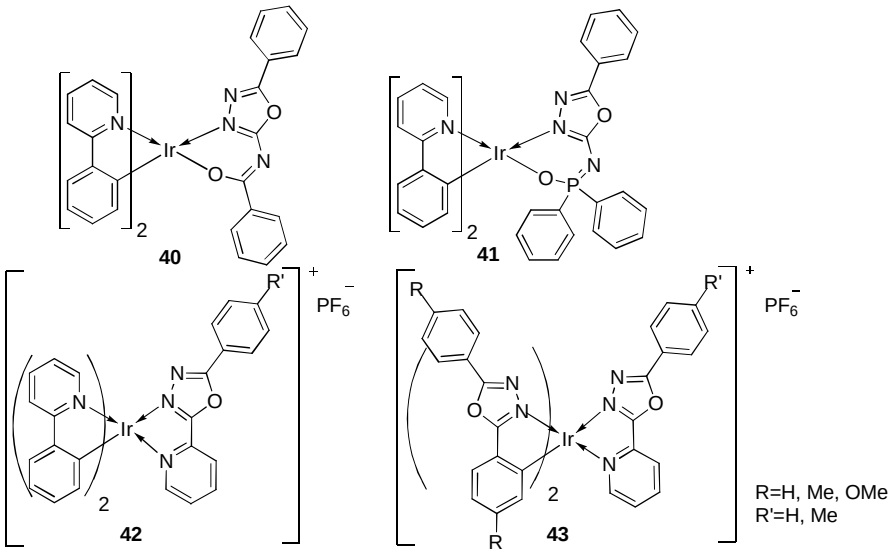
Scheme 12

Recently,[96] Ir(III) complexes **40** bearing the oxadiazole-substituted amide ligand or complex **41** (Scheme 13) were tested and provided good results in construction of green phosphorescent devices, while the cationic iridium(III) complexes **42** and **43** (Scheme 13) were used to prepare yellow and red electroluminescent efficient devices.[97]

Polymer LEDs[98] are advantageous to built single layer devices and such macromolecules containing the oxadiazole ring, combined with electron-donor moieties have been synthesized and studied. Recent examples include red[99] phosphorescent OLEDs based on fluorene/oxadiazole copolymers containing a side-chain Ir(III) complex, copolymers of carbazole and methacrylate derived monomers functionalized with pendent oxadiazole moieties[100] or green[101] phosphorescent OLEDs based on carbazole/oxadiazole copolymers.

Thermally-activated delayed fluorescence based molecules containing an oxadiazole core (acceptor - A) and a suitable electron-donor moiety such as phenoxazine (donor-D)[102] were developed in a D-A or D-A-D configuration (compounds **44** and **45,** Scheme 14) and yielded superior results to those obtained by

conventional fluorescent materials. In spite of their superior properties, such TADF-based materials are still challenging and only few reported, therefore, we expect a development of the area for the future.



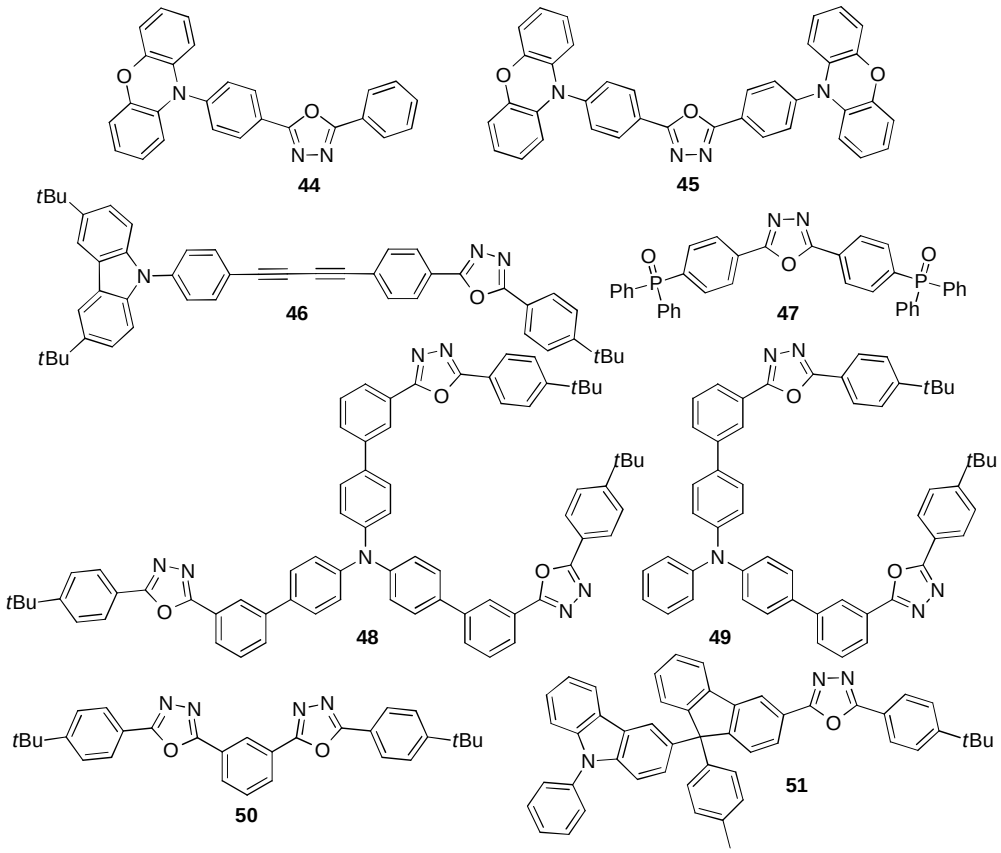
Scheme 13

White light emission has been a subject of deep investigation in the field of optoelectronic devices. It requires mixture of either primary colours (red, green, blue) or complementary colours (i.e. orange and blue).[103] As a result, adequate combination of materials and configuration of the devices must be performed in order to emit the white light. Thus, molecules such as **46**,[104] and **47**[105] have been recently reported to perform well in white emitting devices, having been designed also as donor-acceptor structures. Copolymers containing fluorene and oxadiazole moieties have also been found useful for white electrochemical cells.[106]

The difficulties dealing with the fabrication technology by the vacuum deposition prompted research in finding new compounds that allow fabrication of solution-process devices.[5c] Examples of molecules that allowed use of wet processes with reasonable results are **47**,[105] as well as **48** and **49** (Scheme 14) that were used to obtain phosphorescent OLEDs[107] or compounds **50**[108] and **51**.[109] This new approach is very promising for a more cost-effective fabrication of the optoelectonic devices and there is an increasing number of publications[110] that report improvement of the procedure and step-by-step overcome of the inherent limitations.

3.2.2. Liquid crystals

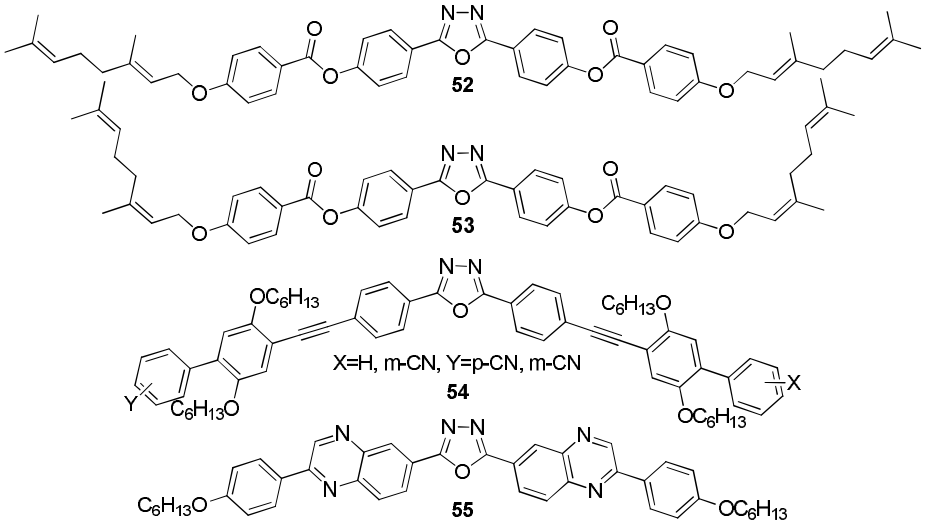
The importance of the liquid crystals in display technology is evidenced by increasing research and study of a wide range of molecules that may lead to feasible and resistant devices. To this end, the 1,3,4-oxadiazole compounds designed to have different types of properties have been synthesized and found to behave as nematic, rod-like or discotic liquid crystals.[111]



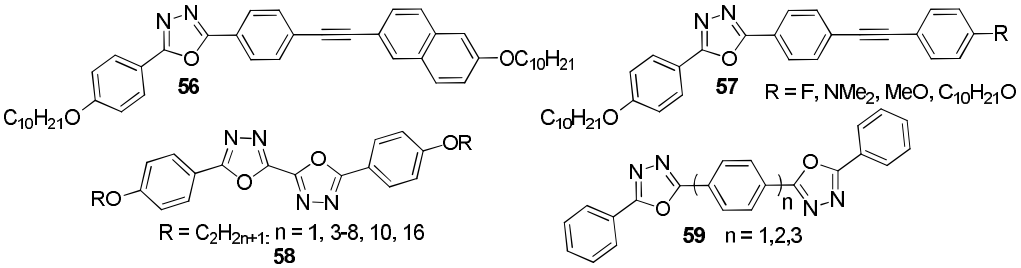
Scheme 14

For example, the *E,E* and *Z,Z* stereoisomers **52** and **53**[112] were investigated for the effect of the configuration on the thermal profile and mesomorphic behaviour, indicating a nematic phase for the *trans–trans* and a lack of mesomorphism for the *cis–cis* stereoisomer. In addition, the V-shaped 1,3,4-oxadiazoles of type **54**[113] were found to behave as nematic liquid crystals bearing shape persistent structures with well-defined bending angles. Another recent example displaying a nematic phase is compound **55**,[114] which also shows blue luminescence (Scheme 15).

One category of molecules that provided rod-like liquid crystals contains the heterocyclic oxadiazole as a central core such as compound **56** (Scheme 16), which also exhibits blue fluorescence and high quantum yields[115] or compounds **57**[116] that have different liquid crystalline behaviours caused by the particular molecular structure and the consequent intermolecular interactions. Other categories of the rod-like liquid crystals include molecules that bear the heterocyclic ring as terminal group[111] or contain more than one heterocyclic rings (compound **58**,[117] Scheme 16), flexible chains or all-aromatic structures (*i.e.* compound **59**,[118] Scheme 16). The luminescent properties of the oxadiazole as well as the high electron mobility led to studies aiming discovery of new luminescent liquid crystals that may find applications for various kinds of optical and electronic devices and such compounds have been recently thoroughly reviewed.[119]



Scheme 15

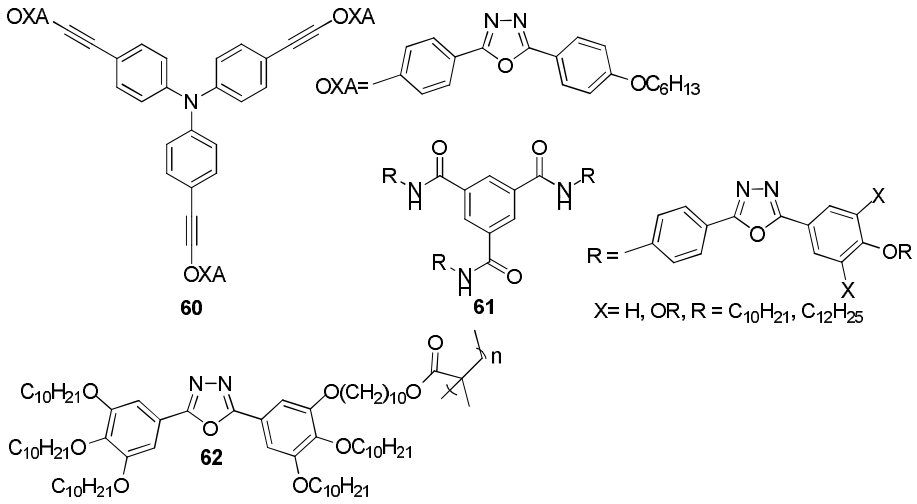


Scheme 16

Discotic liquid crystals have also been reported based on the 1,3,4-oxadiazole core, either as star-shaped or disk-like molecules. For example, compound **60**[120] was found to display a discotic nematic phase attributed mainly to the arm-to-arm interactions between the long rigid arms, while **61** exhibits mesomorphic properties with the increase in the number of the alkoxy chains. [121] Other similar star-shaped compounds have been recently reported[122] bearing also important luminescent properties that were studied in detail. A bis-oxadiazole of type **58** (Scheme 16), bearing 3,4,5-alcoxy-substituted phenyls made the subject of more reports[123] which showed a behaviour of columnar mesophase, but also that it is able to self-assemble to nanoparticles and further to helical nanofibers in DMSO or to form a helical fibrous organogel in DMF. The liquid crystal behaviour was also accompanied by interesting luminescent properties that changed upon the self-assembly processes.

Examples of liquid crystals based on the 1,3,4-oxadiazole compounds are numerous and polycatenar, dimer or polymeric compounds are worth mentioning.[111] Among recent examples, polymer **62** (Scheme 17) exhibited a discotic behaviour and a very good photoluminescence profile compared to the monomer.[124]

Similar to the electroluminescent devices, the research area of the liquid crystals is continously developing and the use of the oxadiazole-based compounds for discovery of new materials with improved properties is open for new accomplishments.



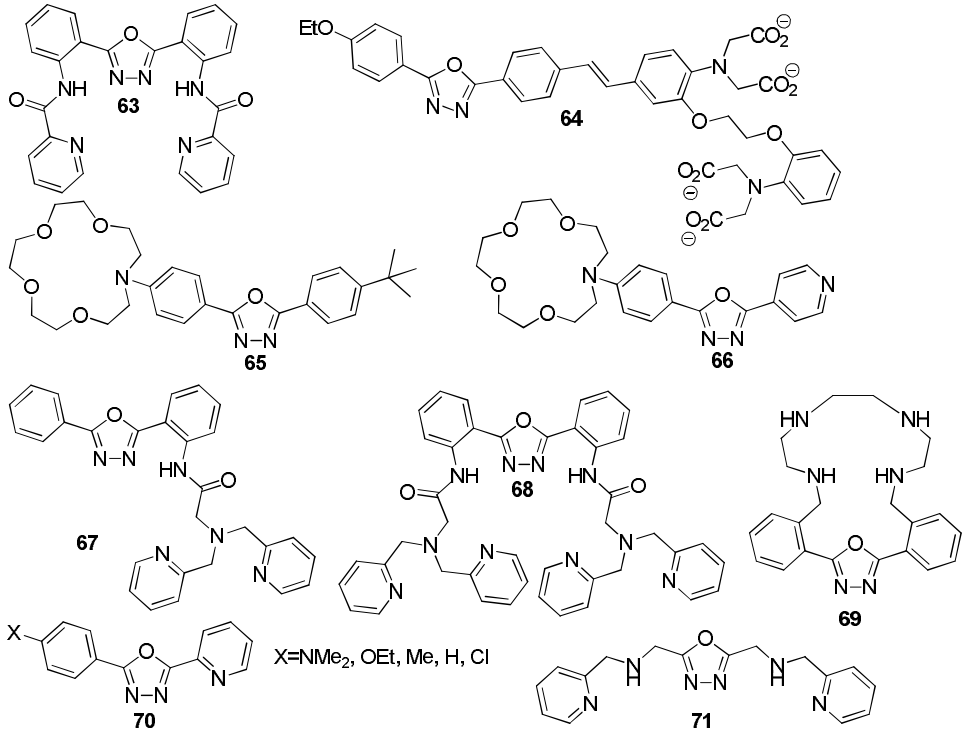
Scheme 17

3.2.3. Sensors for cations and anions, metal-ion complexes and coordination polymers

The presence of the pyridine-like nitrogen atoms of the oxadiazole core imprints at a first sight a coordinating behaviour of such compounds and prompted studies regarding their use as organic ligands for metal-ion complexes and coordination polymers. However, the coordinating abilities of the two nitrogen atoms are not sufficient to provide stable complexes in the absence of other atoms/functional groups and the ligands found applications mainly as sensors for metal-ions.

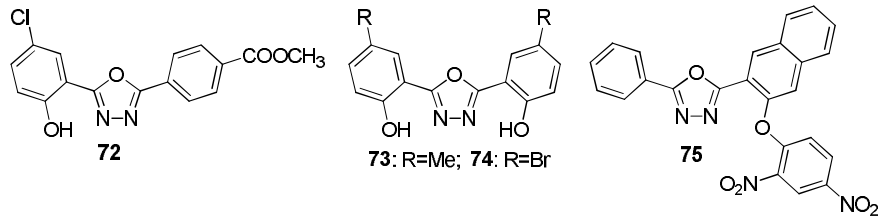
For example, compound **63** (Scheme 18) was shown to selectively bind Ag(I) in a stoechiometry ligand to metal-ion of 1:1 and behave as fluorescence turn-on sensor (λ_{exc}=269 nm and λ_{em}=372 nm) in aqueous solution.[125] In addition, hybrid oxadiazole-BAPTA **64** (Scheme 18) was found to be selective emission ratiometric probe for detection of intracellular Ca(II), with a K_d=0.56 for the metal-ion complex (stoichiometry 1:1) and an emission wavelength maximum at λ_{em}=582 nm.[126] A similar compound based on hybrid-BAPTA moieties was also found to be selective for Cd(II) with low detection limit in aqueous solution, useful for Cd(II) imaging in living cells.[127] Compounds **65** and **66** were reported as intramolecular charge transfer (ICT) probes[128] and found to strongly bind Ca(II) according to the size cavity, while ligands **67**[129] and **68**[130] were reported as selective sensor for recognition of Zn^{2+} in water, yielding complexes with the stoechiometry ligand: metal ion of 1:1 for **67** and 1:2 for **68**, respectively and whose fluorescent emission properties are red-shifted compared to the ligand. Azamacrocycles of type **69**[131] were also found to selectively bind Zn(II) ions in aqueous medium, even in presence of Cd(II) and Pb(II) and behave as fluorescent ON-OFF sensors. A study regarding the coordination properties of ligands **70**[132] toward Ni(II), Cu(II), Zn(II), Cd(II), Hg(II) and Pb(II) revealed fluorescence response profiles varying upon the substituent X with the unsubstituted ligand acting as a fluorescent switch. Recently, oxadiazole **71** was used as ligand

for Fe(II) ions to yield dinuclear complexe[133] that show spin crossover behaviour with hysteresis upon cooling.



Scheme 18

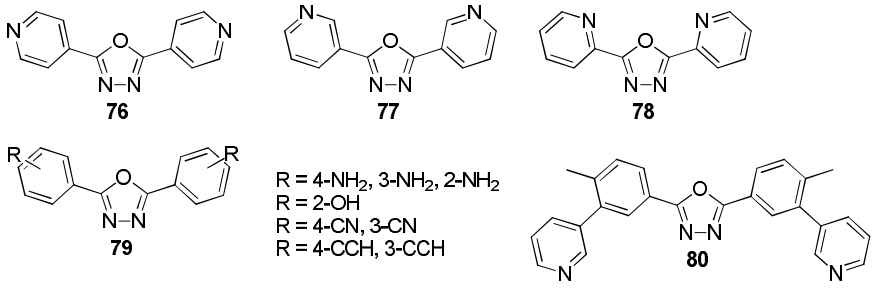
In addition, chemosensors for anions were developed based on *o*-hydroxyphenyl substituted oxadiazoles and the excited state intramolecular proton transfer (ESIPT) processes that occur in case of such compounds. Thus, compounds of type **72**,[134] **73**[135] and **74**[136] (Scheme 19) were reported as selective colorimetric sensors of fluoride in organic solvents, resulting in a colour shift from colourless to yellow upon addition of the anion, while compound **75** was found useful for selective detection of hydrogen sulphide anion.[137]



Scheme 19

Coordination polymers based on oxadiazole ligands substituted with moieties able to coordinate or to enforce the coordinating abilities of the pyridine-like nitrogens of the heterocyclic cores have also been reported.[138] Pyridyl isomers are among the most encountered substituents in the structure of the disubstituted oxadiazoles that yield coordination polymers in which the oxadiazole nitrogen atoms may not be involved or participate with one or both atoms to the metal centre coordination.[139] For examples, the 4-pyridyl-oxadiazole **76** (Scheme 20) yielded 1D, 2D or 3D coordination polymers with various topologies in presence of Cu(I),[140] Mn(II)/Fe(II)/Co(II),[141] Zn(II),[142] Hg(II)[143] or Ag(I).[144] The 3-pyridyl moiety (compound **77**, Scheme 20) has also been used to construct coordination polymers with Cd(II) and Zn(II) ions and benzene dicarboxylate ligands,[145] or with Cu(II) ions and bipyridine,[146] while compound **78** (Scheme 20) containing the 2-pirydyl core was reported to yield complexes of type $[Fe^{II}(L)_2(NCS)_2]$.[147]

Other functional groups such as amino,[148] nitrile[149] or the triple bond[150] (compounds of type **79**, Scheme 20) were used for coordination of Ag(I), yielding interesting topologies that were thoroughly characterised also for the luminescence behaviour. Recent selected examples include coordination polymers derived from ligand **80** and Cd(II) ions,[151] which exhibits the anion-responsive photoluminescence, as well as various iridium complexes of oxadiazole-based compounds, either dinuclear and mononuclear cyclometalated type[152] or in combination with acetylacetonate[153] and *fac*-tris(2-phenylpyridine) ligands.[154]



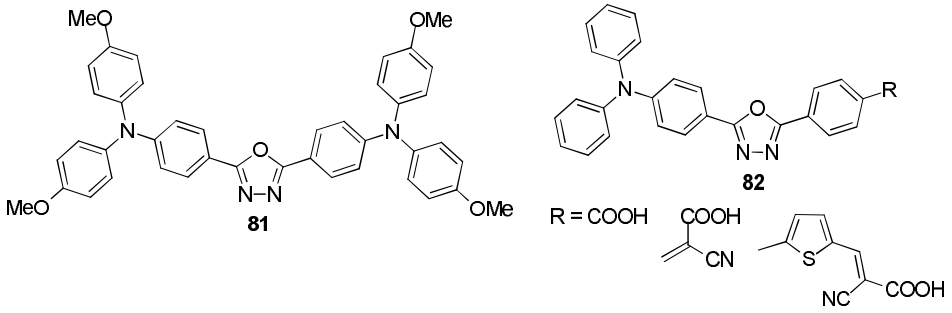
Scheme 20

3.2.4 Others

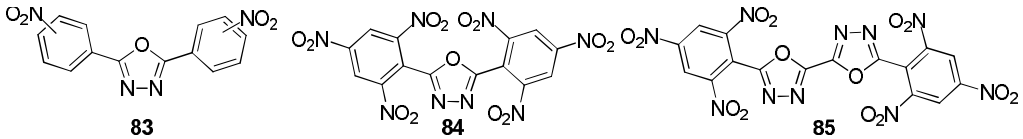
Among the emerging applications of the 1,3,4-oxadiazole compounds, their use as hole transporting molecules in solar cells has recently increasingly attracted. For example, compound **81** (Scheme 21) was used as hole transporting molecule in $CH_3NH_3PbBr_3$ perovskite solar cells yielding an efficiency slightly higher than the reference spirobifluorene compound (Spiro-OMeTAD).[155] In addition, compounds of type **82** (Scheme 21) were designed[156] as donor-π-acceptor molecules to work as efficient sensitizers in dye-sensitized solar cells. Study of their properties indicated good photophysical properties and charge transfer ability upon excitation as well as suitable redox potentials to be further considered as organic sensitizers.

Besides all the aforementioned applications, in seeking highly energetic materials, useful for novel formulations of propellants and explosives, the nitrogen enriched oxadiazole compounds, seem to meet the basic requirements of such molecules: high thermal and chemical stability, a low sensitivity to shocks and a low oxygen balance.[157] Thus, series of variously nitro-substituted compounds of type **83** (Scheme 22) were synthesized and the specific parameters calculated. In addition, starting from the earlier reported **84** (Scheme 22) that was found to have a decomposition temperature much higher than that of HNBP (2,2',4,4',6,6'-

hexanitrobiphenyl),[158] compound **85** (Scheme 22) was very recently synthesized and showed good detonation parameters, low sensitivity values and a high decomposition temperature, desirable properties for thermally stable explosives.[159]



Scheme 21



Scheme 22

4. Conclusions

The field of the 1,3,4-oxadiazole-based compounds has achieved a long transfer from the incipient studies regarding their synthesis to complex investigations regarding structural particularities and the consequences over the chemical reactivity and usefulness for a wide range of applications. Nowadays, we are dealing with numerous synthetic methods that have each their advantages and drawbacks and are suitable for specific applications. Starting from the early reported harsh dehydrative cyclisations of the *N*,*N*′-diacylhydrazines and cycloaddition of tetrazoles to acid chlorides, we are now able to efficiently construct the heterocyclic core, by use of mild reagents, through oxidative cyclisations of the convenient *N*-acylhydrazones or cross-coupling reactions of the already closed heterocycle with various electrophilic or nucleophilic reagents, under transition metal catalysis. Thus, a wide range of structures may be available for applications in different areas.

The biological activity of the 1,3,4-oxadiazole congeners has always been a subject of interest, evidenced by the commercially available antiviral drug on the market and a potent anticancer drug in the final phases of the clinical trials. Among the greatest achievements in the area of materials chemistry, one can note use of the compounds as electron transporting molecules for construction of fluorescent, phosphorescent or thermally-activated delayed fluorescence OLEDs. The field is under a continuous development and we expect to further open new ways in the chemistry of the oxadiazoles.

Apart from these two great areas of research, the properties of the oxadiazoles were tuned to allow preparation of sensors for various cations and anions, useful both for chemical and biochemical systems,

liquid crystals and coordination polymers, as well as the newly approached fields of solar cells and highly energetic materials.

We are, therefore, entitled to believe that the chemistry of the 1,3,4-oxadiazoles will continue to bring great achievements in various fields at the boundaries with biology and physics and to be encouraged that deeper and unlimited investigations will make this chemistry a pleasant and unforeseeable journey.

Acknowledgments

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References

1. Eicher, T.; Hauptmann, S.; Speicher, A. *The Chemistry of Heterocycles, Structure, Reactions, Syntheses, and Applications, Second Edition*, **2003** Wiley-VCH.
2. (a) Zhou, Y.; Wang, J.; Gu, Z.; Wang, S.; Zhu, W.; Aceña, J. L.; Soloshonok, V. A.; Izawa, K.; Liu, H. *Chem. Rev.* **2016**, *116*, 422; (b) Summa, V.; Petrocchi, A.; Bonelli, F.; Crescenzi, B.; Donghi, M.; Ferrara, M.; Fiore, F.; Gardelli, C.; Gonzalez Paz, O.; Hazuda, D. J.; Jones, P.; Kinzel, O.; Laufer, R.; Monteagudo, E.; Muraglia, E.; Nizi, E.; Orvieto, F.; Pace, P.; Pescatore, G.; Scarpelli, R.; Stillmock, K.; Witmer, M. V.; Rowley, M. *J. Med. Chem.* **2008**, *51*, 5843.
3. Barry, P. J.; Jones, A. M. *Drugs* **2015**, *75*, 1165.
4. Adachi, C.; Tsutsui, T.; Saito, S. *Appl. Phys. Lett*. **1990**, *56*, 799.
5. (a) Paun, A.; Hadade, N. D.; Paraschivescu C. C.; Matache, M. *J. Mater. Chem. C* **2016**, *4*, 8596; (b) Yang, X.; Xu, X.; Zhou, G. *J. Mater. Chem. C* **2015**, *3*, 913; (c) Tao, Y.; Yang, C.; Qin, J. *Chem. Soc. Rev.* **2011**, *40*, 2943; (d) Hughes, G.; Bryce, M. R. *J. Mater. Chem.* **2005**, *15*, 94; (e) Kulkarni, A. P.; Tonzola, C. J.; Babel, A.; Jenekhe, S. A. *Chem. Mater.* **2004**, *16*, 4556.
6. Wei, H.; He, C.; Zhang, J.; Shreeve, J. M. *Angew. Chem. Int. Ed.* **2015**, *54*, 9367.
7. Katritzky, A.; Pozharskii, F. A. *Handbook of Heterocyclic Chemistry, 2nd Edition*, **2000**, Academic Press.
8. (a) Khan, I.; Ibrar, A.; Abbas, N.; *Arch. Pharm. Chem. Life Sci.* **2013**, *346*, 1; (b) Soares de Oliveira, C.; Lira, B. F.; Barbosa-Filho, J. M.; Fernandez Lorenzo, J. G.; Filgueiras de Athayde-Filho, P. *Molecules* **2012**, *17*, 10192.
9. (a) Gnanasekaran, K. K.; Nammalwar, B.; Murie, M.; Bunce, R. A. *Tetrahedron Lett.* **2014**, *55*, 6776; (b) Kudelko, A.; Zielinski, W. *Tetrahedron Lett.* **2012**, *53*, 76; (c) Polshettiwar, V.; Varma, R. S. *Tetrahedron Lett.* **2008**, *49*, 879; (d) Ainsworth, C. *J. Am. Chem. Soc.* **1955**, *77*, 1148.
10. Fan, Y.; He, Y.; Liu, X.; Hu, T.; Ma, H.; Yang, X.; Luo, X.; Huang, G. *J. Org. Chem.* **2016**, *81*, 6820.
11. Gao, Q.; Liu, S.; Wu, X.; Zhang, J.; Wu, A. *Org. Lett.* **2015**, *17*, 2960.
12. Souldozi, A.; Ramazani, A. *Tetrahedron Lett.* **2007**, *48*, 1549.
13. Kitahara, M.; Hirano, K.; Tsurugi, H.; Satoh, T.; Miura, M. *Chem. Eur. J.* **2010**, *16*, 1772.
14. (a) Theunissen, C.; Evano, G. *Org. Lett.* **2014**, *16*, 4488; (b) Besselivre, F.; Piguel, S. *Angew. Chem. Int. Ed.* **2009**, *48*, 9553.
15. Kawano, T.; Matsuyama, N.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2010**, *75*, 1764.
16. Reddy, G. C.; Balasubramanyam, P.; Salvanna, N.; Das, B. *Eur. J. Org. Chem.* **2012**, 471.
17. Das, B.; Reddy, G. C.; Balasubramanyam, P.; Salvanna, N. *Tetrahedron* **2012**, *68*, 300.
18. Salvanna, N.; Reddy, G. C.; Rao, B. R.; Das, B. *RSC Adv.* **2013**, *3*, 20538.
19. Mukai, T.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett.* **2010**, *12*, 1360.
20. Salvanna, N.; Das, B. *Synlett* **2014**, *25*, 2033.

21. (a) Dannenberg, C. A.; Bizet, V.; Zou, L.-H.; Bolm, C. *Eur. J. Org. Chem.* **2015**, 77; (b) Wunderlich, S. H.; Knochel, P. *Angew. Chem. Int. Ed.* **2007**, *46*, 7685; (c) Zhao, X.; Ding, F.; Li, J.; Lu, K.; Lu, X.; Wang, B.; Yu, P. *Tetrahedron Lett.* **2015**, *56*, 511.
22. (a) Zarudnitskii, E. V.; Pervak, I. I.; Merkulov, A. S.; Yurchenko, A. A.; Tolmachev, A. A; Pinchuka, A. M. *Synthesis* **2006**, 1279; (b) Zarudnitskii, E. V.; Pervak, I. I.; Merkulov, A. S.; Yurchenko, A. A.; Tolmachev, A. A; *Tetrahedron* **2008**, *64*, 10431.
23. (a) Tadikonda, R.; Nakka, M.; Rayavarapu, S.; Kalidindi, S. P. K.; Vidavalur, S. *Tetrahedron Lett.* **2015**, *56*, 690; (b) Kawano, T.; Yoshizumi, T.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett.* **2009**, *11*, 3072.
24. (a) Salvanna, N.; Reddy, G. C.; Das, B. *Tetrahedron* **2013**, *69*, 2220; (b) Hachiya, H.; Hirano, K.; Satoh, T.; Miura, M. *ChemCatChem* **2010**, *2*, 1403.
25. Zou, L.-H.; Mottweiler, J.; Priebbenow, D. L.; Wang, J.; Stubenrauch, J. A.; Bolm, C. *Chem. Eur. J.* **2013**, *19*, 3302.
26. (a) Yang, S. J.; Lee, S. H.; Kwak, H. J.; Gong, Y.-D. *J. Org. Chem.* **2013**, *78*, 438;. (b) Piatnitski Chekler, E. L.; Elokdah, H. M.; Butera, J. *Tetrahedron Lett.* **2008**, *49*, 6709.
27. Rivera, N. R.; Balsells, J.; Hansen, K. B. *Tetrahedron Lett.* **2006**, *47*, 4889.
28. Dolman, S. J.; Gosselin, F.; O'Shea, P. D.; Davies, I. W. *J. Org. Chem.* **2006**, *71*, 9548.
29. Maghari, S.; Ramezanpour, S.; Darvish, F.; Balalaie, S.; Rominger, F.; Bijanzadeh, H. R. *Tetrahedron* **2013**, *69*, 2075.
30. Li, Z.; Gu, Z.; Yin, K.; Zhang, R.; Deng, Q.; Xiang, J. *Eur. J. Med. Chem.* **2009**, *44*, 4716.
31. (a) Chen, C.-J.; Song, B.-A.; Yang, S.; Xu, G.-F.; Bhadury, P.S.; Jin, L.-H.; Hu, D.-Y.; Li, Q.-Z.; Liu, F.; Xue, W.; Lu, P.; Chen, Z. *Bioorg. Med. Chem.* **2007**, *15*, 3981; (b) Dai, C.; Xu, Z.; Huang, F.; Yu, Z.; Gao, Y.-F. *J. Org. Chem.* **2012**, *77*, 4414.
32. Liu, K.; Lu, X.; Zhang, H.-J.; Sun, J.; Zhu, H.-L. *Eur. J. Med. Chem.* **2012**, *47*, 473.
33. Niu, L.-F.; Cai, Y.; Liang, C.; Hui, X.-P.; Xu, P.-F. *Tetrahedron*, **2011**, *67*, 2878.
34. (a) Patel, K. D.; Prajapati, S. M.; Panchal, S. N.; Patel, H. D. *Synth. Commun.* **2014**, *44*, 1859; (b) Jakopin, Z.; Dolenc, M. S. *Curr. Org. Chem.* **2008**, *12*, 850.
35. (a) Li, A. F.; Ruan, Y. B.; Jiang, Q. Q.; He, W. B.; Jiang, Y. B. *Chem. Eur. J.* **2010**, *16*, 5794; (b) Zhang, Y.; Zuniga, C.; Kim, S. J.; Cai, D.; Barlow, S.; Salman, S.; Coropceanu, V.; Brédas, J. L.; Kippelen, B.; Marder, S. *Chem. Mater.* **2011**, *23*, 4002; (c) Paraschivescu, C. C.; Dumitrascu, F.; Draghici, C.; Ruta, L. L.; Matache, M.; Baciu, I.; Dobrota, C. *Arkivoc*, **2008**, *XIII*, 198; (d) Al-Talib, M.; Tashtoush, H.; Odeh, N. *Synth. Commun.* **1990**, *20*, 1811.
36. Borg, S.; Vollinga, R. C.; Labarre, M.; Payza, K.; Terenius, L.; Luthman, K. *J. Med. Chem.* **1999,** *42*, 4331.
37. Sharma, G.; Begum, A.; Rakesh, K.; Palakodety, R. *Synth. Commun.* **2004**, *34*, 2387.
38. Ellis, D.; Johnson, P.S.; Nortcliffe, A.; Wheeler, S. *Synth. Commun.* **2010**, 40, 3021.
39. Pouliot, M. F.; Angers, L.; Hamel, J. D.; Paquin, J. F. *Org. Biomol. Chem.* **2012**, *10*, 988.
40. Dabiri, M.; Salehi, P.; Baghbanzadeh, M.; Bahramnejad, M. *Tetrahedron Lett.* **2006**, *47*, 6983.
41. (a) Stephanatou, J. S. *J. Heterocyclic Chem.* **1983**, *20*, 845; (b) Rekkas, S.; Rodios, N.; Alexandrou, N. E. *Synthesis* **1984**, 602; (c) Rekkas, S.; Rodios, N.; Alexandrou, N. E. *Synthesis* **1986**, 411.
42. Elwahy, A. H. M.; Ahmed, M. M.; El-Sadek, M. *J. Chem. Res. (S)* **2001**, 175.
43. Guin, S.; Ghosh, T.; Rout, S. K.; Banerjee, A.; Patel, B. K. *Org. Lett.* **2011**, *13*, 5976.
44. (a) Yoshimura, A., Zhdankin, V. V. *Chem. Rev.* **2016**, *116*, 3328; (b) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2008**, *108*, 5299.
45. Yang, R-.Y.; Dai, L.-X. *J. Org. Chem.* **1993**, *58*, 3301.

46. (a) Paraschivescu, C. C.; Hadade, N. D.; Coman, A. G.; Gautier, A.; Cisnetti, F.; Matache, M. *Tetrahedron Lett.* **2015**, *56*, 3691; (b) Paraschivescu, C.; Matache, M; Dobrotă, C.; Nicolescu, A.; Maxim, C.; Deleanu, C.; Fărcășanu, I.C.; Hãdade, N. D. *J. Org. Chem.* **2013**, *78*, 2670; (c) Shang, Z. *Synth. Commun.* **2006**, *36*, 2927.
47. Dobrota, C.; Paraschivescu, C. C.; Dumitru, I.; Matache, M.; Baciu, I.; Ruta, L.L. *Tetrahedron Lett.* **2009**, *50*, 1879.
48. (a) Majji, G.; Rout, S. K.; Guin, G.; Gogoi, A.; Patel, B. K. *RSC Advances*, **2014**, *4*, 5357; (b) Yu, W.; Huang, G.; Zhang, Y.; Liu, H.; Dong, L.; Yu, X.; Li, Y.; Chang J. *J. Org. Chem.* **2013**, *78*, 10337; (c) Guin, S.; Rout, S. K.; Ghosh, T.; Khatun, N.; Patel, B. K. *RSC Advances* **2012**, *2*, 3180.
49. (a) Paun, A.; Matache, M.; Enache, F.; Nicolau, I.; Paraschivescu, C. C.; Ionita, P.; Zarafu, I.; Parvulescu, V. I.; Guillaumet, G. *Tetrahedron Lett.* **2015**, *56*, 5349; (b) Paraschivescu, C. C.; Hadade, N. D.; Coman, A. G.; Gautier, A.; Cisnetti, F.; Matache, M. *Tetrahedron Lett.* **2015**, *56*, 3691.
50. (a) Stabile, P.; Lamonica, A.; Ribecai, A.; Castoldi, D.; Guercio, G.; Curcuruto, O. *Tetrahedron Lett.* **2010**, *51*, 4801; b) Augustine, J. K.; Vairaperumal, V.; Narasimhan, S.; Alagarsamy, P.; Radhakrishnan, A. *Tetrahedron* **2009**, *65*, 9989; (c) Li, C.; Dickson, H. D. *Tetrahedron Lett.* **2009**, *50*, 6435.
51. Wang, L.; Cao, J.; Chen, Q.; He, M. *J. Org. Chem.* **2015**, *80*, 4743.
52. Lia, Z.; Wang, L. *Adv. Synth. Catal.* **2015**, *357*, 3469.
53. Fan, X.-Y.; Jiang, X.; Zhang, Y.; Chen, Z.-B.; Zhu, Y.-M. *Org. Biomol. Chem.* **2015**, *13*, 10402.
54. Shang, Z.; Chua, Q.; Tan, S. *Synthesis* **2015**, *47*, 1032.
55. Shang, Z.; Reiner, J.; Chang, J.; Zhao, K. *Tetrahedron Lett.* **2005**, *46*, 2701.
56. (a) Chidirala, S.; Ulla, H.; Valaboju, A.; Kiran, M. R.; Mohanty, M. E.; Satyanarayan, M. N.; Umesh, G.; Bhanuprakash, K.; Rao, V. J. *J. Org. Chem.* **2016**, *81*, 603; (b) Reichart, B.; Kappe, C. O. *Tetrahedron Lett*. **2012**, *53*, 952; (c) Yang, C.-C.; Hsu, C.-J.; Chou, P.-T.; Cheng, H. C.; Su, Y. O.; Leung, M. *J. Phys. Chem. B* **2010**, *114*, 756; (d) Chien, Y.-Y.; Wong, K.-T.; Chou, P-T.; Cheng, Y.-M. *Chem. Commun.* **2002**, 2874.
57. Kettner, M. A.; Klapçtke, T. M.; Witkowski, T. G.; von Hundling, F. *Chem. Eur. J.* **2015**, *21*, 4238.
58. Tan, T. M. C.; Chen, Y.; Kong, K. H.; Bai, J.; Li, Y.; Lim, S. G.; Ang, T. H.; Lam, Y. *Antivir. Res.* **2006**, *71*, 7.
59. Zuo, W. Q.; Wang, N. Y.; Zhu, Y.; Liu, L.; Xiao, K. J.; Zhang, L. D.; Gao, C.; Liu, Z.-H.; You, X.-Y.; Shi, Y.-J.; Peng, C.-T.; Ran, K.; Tang, H. Yu, L.-T. *RSC Adv.* **2016**, *6*, 40277.
60. James, N. D.; Growcott, J. W. *Drugs Future* **2009**, *34*, 624.
61. Kamal, A.; Srikanth, Y. V. V.; Shaik, T. B.; Khan, M. N. A.; Ashraf, M.; Reddy, M. K.; Kumar, K. A.; Kalivendi, S. V. *Med. Chem. Commun.* **2011**, *2*, 819.
62. Formagio, A. S. N.; Tonin, L. T. D.; Foglio, M. A.; Madjarof, C.; de Carvalho, J. E.; da Costa, W. F.; Cardoso, F. P.; Sarragiotto, M. H. *Bioorg. Med. Chem.* **2008**, *16*, 9660.
63. Kamal, A.; Srikanth, P. S.; Vishnuvardhan, M. V. P. S.; Bharath Kumar, G.; Suresh Babu, K.; Ali Hussaini, S. M.; Kapure, J. S.; Alarifi, A. *Bioorg. Chem.* **2016**, *65*, 126.
64. Garg, S.; Raghav, N. *Bioorg. Chem.* **2016**, *67*, 64.
65. Palmer, J. T.; Hirschbein, B. L.; Cheung, H.; McCarter, J.; Janc, J. W.; Yu, W. Z.; Wesolowski, G. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 2909.
66. Khan, M. T.; Choudhary, M. I.; Khan, K. M.; Rani, M.; Rahman, A. U. *Bioorg. Med. Chem.* **2005**, *13*, 3385.
67. Khan, K. M.; Rani, M.; Ambreen, N.; Ali, M.; Hussain, S.; Perveen, S.; Choudhary, M. I. *Med. Chem. Res.* **2013**, *22*, 6022.

68. Naerum, L.; Norskov-Lauritsen, L.; Olesen, P. H. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 525.
69. Lukas, T. J.; Schiltz, G. E.; Arrat, H.; Scheidt, K.; Siddique, T. *Bioorg. Med. Chem. Lett.* **2014**, *24*, 1532.
70. Bansal, S.; Bala, M.; Suthar, S. K.; Choudhary, S.; Bhattacharya, S.; Bhardwaj, V.; Singla, S.; Joseph, A. *Eur. J. Med. Chem.* **2014**, *80*, 167.
71. Grover, J.; Bhatt, N.; Kumar, V.; Patel, N. K.; Gondaliya, B. J.; Sobhia, M. E.; Bhutania, K. K.; Jachak, S. M. *RSC Adv.* **2015**, *5*, 45535.
72. Guimaraes, C. R. W.; Boger, D. L.; Jorgensen, W. L. *J. Am. Chem. Soc.* **2005**, *127*, 17377.
73. (a) Boström, J.; Hogner, A.; Llinàs, A.; Wellner, E.; Plowright, A. T. *J. Med. Chem.* **2012**, *55*, 1817; (b) Scott, J. S.; Birch, A. M.; Brocklehurst, K. J.; Brown, H. S.; Goldberg, K.; Groombridge, S. D.; Hudson, J. A.; Leach, A. G.; MacFaul, P. A.; McKerrecher, D.; Poultney, R.; Schofield, P.; Svenssonb, P. H. *Med. Chem. Commun.* **2013**, *4*, 95.
74. Rachakonda, V.; Alla, M.; Kotipalli, S. S.; Ummanni, R. *Eur. J. Med. Chem.* **2013**, *70*, 536.
75. Zhang, M. Z.; Mulholland, N.; Beattie, D.; Irwin, D.; Gu, Y.-C.; Chen, Q.; Yang, G. F.; Clough, J. *Eur. J. Med. Chem.* **2013**, *63*, 22.
76. Reddy, G. D.; Park, S. J.; Cho, H. M.; Kim, T. J.; Lee, M. E. *J. Med. Chem.* **2012**, *55*, 6438.
77. (a) Jou, J.-H; Kumar, S.; Agrawal, A.; Lia, T.-J.; Sahoo, S. *J. Mater. Chem. C* **2015**, *3*, 2974; (b) Ingram, G.; Nguyen, C.; Lu, Z.-H. *J. Photon. Energy* **2015**, *5*, 050998.
78. Tao, Y.; Yuan, K.; Chen, T.; Xu, P.; Li, H.; Chen, R.; Zheng, C.; Zhang, L.; Huang, W. *Adv. Mater.* **2014**, *26*, 7931.
79. Ho, S.; Liu, S.; Chen, Y.; So, F. *J. Photon. Energy* **2015**, *5*, 057611.
80. Yook, K. S.; Lee, J. Y. *Adv. Mater.* **2014**, *26*, 7931.
81. Tamoto, N.; Adachi, C.; Nagai, K. *Chem. Mater.* **1997**, *9*, 1077.
82. (a) Antoniadis, H.; Inbasekaran, M.; Woo, E. P. *Appl. Phys. Lett.* **1998**, *73*, 3055; (b) Ahn, J. H.; Wang, C.; Pearson, C.; Bryce, M. R.; Petty, M. C. *Appl. Phys. Lett.* **2004**, *85*, 1283.
83. Mikroyannidis, J. A.; Spiliopoulos, I. K.; Kasimis, T. S.; Kulkarni, A. P.; Jenekhe, S. A. *Macromolecules* **2003**, *36*, 9295.
84. (a) Chen, R.-T.; Chen, S.-H.; Hsieh, B.-Y.; Chen, Y. *J. Pol. Sci. A Pol. Chem.* **2009**, *47*, 2821; (b) Chen, R.-T.; Su, W.-F.; Chen, Y. *J. Pol. Sci. A Pol. Chem.* **2011**, *49*, 184; (c) Kim, Y.-H.; Park, S.-J.; Park, J.-W.; Kim, J. H.; Kwon, S.-K. *Macromolec. Res.* **2007**, *15*, 216.
85. Wu, C.-L.; Chang, C.-H.; Chang, Y.-T.; Chen, C.-T.; Chen, C.-T.; Su, C.-J. *J. Mater. Chem. C* **2014**, *2*, 7188.
86. (a) Shih, C.-H.; Rajamalli, P.; Wu, C.A.; Hsieh, W. T.; Cheng, C. H. *ACS Appl. Mater. Interfaces* **2015**, *7*, 10466; (b) Shih, C.-H.; Rajamalli, P.; Wu, C. A.; Chiu, M. J.; Chu, L. K.; Cheng, C.-H. *J. Mater. Chem. C* **2015**, *3*, 1491.
87. Fan, C.; Lei, Y.; Liu, Z.; Wang, R.; Lei, Y.; Li, G.; Xiong, Z.; Yang, X. *ACS Appl. Mater. Interfaces* **2015**, *7*, 20769.
88. Leung, M.-K.; Yang, C.-C.; Lee, J.-H.; Tsai, H.-H.; Lin, C.-F.; Huang, C.-Y.; Su, Y.O.; Chiu, C.-F. *Org. Lett.* **2007**, *9*, 235.
89. For a review see: Sun, D.; Ren, Z.; Bryce, M.R.; Yan, S. *J. Mater. Chem. C* **2015**, *3*, 9496. For selected example see: Leung, M.; Yang, W.-H.; Chuang, C. N.; Lee, J. H.; Lin, C. F.; Wei, M. K.; Liu, Y. H. *Org. Lett.* **2012**, *14*, 4986.
90. (a) Liao, Y.-L.; Lin, C.-Y.; Wong, K.-T.; Hou, T.-H.; Hung, W.-Y. *Org. Lett.* **2007**, *9*, 4511; (b) Zheng, Y.; Batsanov, A. S.; Jankus, V.; Dias, F. B.; Bryce, M. R.; Monkman, A. P. *J. Org. Chem.*

2011, *76*, 8300; (c) Chidirala, S.; Ulla, H.; Valaboju, A.; Kiran, M. R.; Mohanty, M. E.; Satyanarayan, M. N.; Umesh, G.; Bhanuprakash, K.; Rao, V. J. *J. Org. Chem.* **2016**, *81*, 603.

91. For a review see: Dumur, F.; Goubard, F. *New J. Chem.* **2014**, 38, 2204. For selected example see: Zhang, S.; Xu, Q.-L.; Xia, J. C.; Jing, Y.-M.; Zheng, Y.-X. Zuo, J.-L. *New J. Chem.* **2015**, *39*, 7954.
92. Tao, Y.; Wang, Q.; Yang, C.; Wang, Q.; Zhang, Z.; Zou, T.; Qin, J.; Ma, D. *Angew. Chem. Int. Ed.* **2008**, *47*, 8104.
93. Tao, Y.; Ao, L.; Wang, Q.; Zhong, C.; Yang, C.; Qin J.; Ma, D. *Chem. Asian J.* **2010**, *5*, 278.
94. Zhu, M.; Ye, T.; Li, C.-G.; Cao, X.; Zhong, C.; Ma, D.; Qin, J.; Yang, C. *J. Phys. Chem. C* **2011**, *115*, 17965.
95. Deshapande, N.; Belavagi, N. S.; Sunagar, M. G.; Gaonkar, S.; Pujar, G. H.; Wari, M. N.; Inamdar, S. R.; Khazi, I. A. M. *RSC Adv.* **2015**, *5*, 86685.
96. Zhang, F.; Li, W.; Jing, Y.; Ma, D.; Zhang, F.; Li, S.; Cao, G.; Li, Z.; Guo, G.; Wei, B.; Zheng, Y.; Zhang, D.; Duan, L.; Wu, Z.; Li, C.; Feng, Y.; Zhai, B. *J. Mater. Chem. C* **2016**, *4*, 5469.
97. Zhang, J.; Zhou, L.; Al-Attar, H. A.; Shao, K.; Wang, L.; Zhu, D.; Su, Z.; Bryce, M. R.; Monkman, A. P. *Adv. Funct. Mater.* **2013**, *23*, 4667.
98. (a) Burroughes, H.; Bradley, D. D. C.; Brown, A. R.; Marks, R. N.; McKay, K.; Friend, R. H.; Burn, P. L.; Holmes, A. B. *Nature*, **1990**, *347*, 539; (b) Grimsdale, A. C.; Chan, K. L.; Martin, R. E.; Jokisz, P. G.; Holmes, A. B. *Chem. Rev.* **2009**, *109*, 897.
99. Deng, J.; Liu, Y.; Wang, Y.; Tan, H.; Zhang, Z.; Lei, G.; Yu, J.; Zhu, M.; Zhu, W.; Cao, Y. *Eur. Pol. J.* **2011**, *47*, 1836.
100. Zdyrko, B.; Bandera, Y.; Tsyalkovsky, V.; Huebner, C. F.; Shetzline, J. A.; Rungta, P.; Roeder, R. D.; Tonkin, C.; Creager, S. E.; Foulger, S. H. *J. Pol. Sci. B: Pol. Phys.* **2015**, *53*, 1663.
101. Pandya, S. U.; Al Attar, H. A.; Jankus, V.; Zheng, Y.; Bryce, M. R.; Monkman, A. P. *J. Mater. Chem.* **2011**, *21*, 18439.
102. (a) Lee, J.; Shizu, K.; Tanaka, H.; Nomura, H.; Yasuda, T.; Adachi, C. *J. Mater. Chem. C* **2013**, *1*, 4599; (b) Lu, J.; Zheng, Y.; Zhang, J. *Phys. Chem. Chem. Phys.* **2015**, 17, 20014.
103. Wu, Z.; Ma, D. *Mater. Sci. Eng. R* **2016**, *107*, 1.
104. Wu, X.; Wang, L.; Hua, Y.; Wang, C.; Batsanov, A. S.; Bryce, M. R. *Tetrahedron* **2014**, *70*, 2015.
105. Liu, R.; Xu, X.; Peng, J.; Yao, C.; Wang, J.; Li, L. *RSC Adv.* **2015**, *5*, 36568.
106. Sun, M.; Zhong, C.; Li, F.; Cao, Y.; Pei, Q. *Macromolecules* **2010**, *43*, 1714.
107. Pu, Y. R.; Chen, Y. *J. Lumines.* **2016**, *170*, 127.
108. Chang, Y.-T; Chang, J.-K.; Lee, Y-T.; Wang, P.-S.; Wu, J.-L.; Hsu, C.-C.; Wu, I.-W.; Tseng, W.-H.; Pi, T.-W.; Chen, C.-T.; Wu, C.-I. *ACS Appl. Mater. Interfaces* **2013**, *5*, 10614.
109. Lin, W.-C.; Lin, H.-W.; Mondal, E.; Wong, K.-T. *Org. Electron.* **2015**, *17*, 1.
110. For other selected examples see: (a) Lee, Y.-T.; Chang, Y.-T.; Lee, M.-T.; Chiang, P.-H.; Chen, C.-T.; Chen, C.-T. *J. Mater. Chem. C* **2014**, *2*, 382; (b) Lü, J.; Ma, Z.; Meng, B.; Sui, D.; Zhang, B.; Xie, Z.; Jing, X.; Wang, F.; Ding, J.; Wang, L. *Opt Express* **2011**, A1241; (c) Jiang, W.; Duan, L.; Qiao, J.; Zhang, D.; Dong, G.; Wang, L.; Qiu, Y. *J. Mater. Chem.* **2010**, *20*, 6131; (d) Ye, S.; Liu, Y.; Lu, K.; Wu, W.; Du, C.; Liu, H.; Wu, T.; Yu, G. *Adv. Funct. Mater.* **2010**, *20*, 3125.
111. Han, J. *J. Mater. Chem. C* **2013**, *1*, 7779.
112. Belaissaoui, A.; Cowling, S. J.; Goodby, J. W. *Liq. Cryst.* **2013**, *40*, 421.
113. Lehmann, M.; Kohn, C.; Kresseb, H.; Vakhovskaya, Z. *Chem. Commun.* **2008**, 1768.
114. Kuo, H.-M.; Chen, Y.-L.; Lee, G.-H.; Lai, K. C *Tetrahedron* **2016**, *72*, 6843.
115. Cristiano, R.; Vieira, A. A.; Ely, F.; Gallardo, H. *Liq. Cryst.* **2006**, *33*, 381.
116. Han, J.; Chui, S. S.-Y.; Che, C.-M. *Chem. Asian J.* **2006**, *1*, 814.

117. Qu, S.; Chen, X.; Shao, X.; Li, F.; Zhang, H.; Wang, H.; Zhang, P.; Yu, Z.; Wu, K.; Wang, Y.; Li, M. *J. Mater. Chem.* **2008**, *18*, 3954.
118. Zafiropoulos, N. A.; Choi, E-J.; Dingemans, T.; Lin, W.; Samulski, E. T. *Chem. Mater.* **2008**, 20, 3821.
119. Wang, Y.; Shi, J.; Chen, J.; Zhu, W.; Baranoff, E. *J. Mater. Chem. C* **2015**, *3*, 7993.
120. Kim, B. G.; Kim, S.; Young Park, S. *Tetrahedron Lett.* **2001**, *42*, 2697.
121. Barberá, J.; Godoy, M. A.; Hidalgo, P. L.; Parra, M. L.; Ulloa, J. A.; Vergara, M. *Liq. Cryst.* **2011**, *38*, 679.
122. (a) Girotto, E.; Eccher, J.; Vieira, A. A.; Bechtold, I. H.; Gallardo, H. *Tetrahedron* **2014**, *70*, 3355; (b) Pradhana, B.; Pathaka, S. K.; Guptaa, R. K.; Guptab, M.; Palb, S. K.; Achalkumar, A. S. *J. Mater. Chem. C* **2016**, *4*, 6117; (c) Westphal, E.; Prehm, M.; Bechtold, I. H.; Tschierske, C.; Gallardo, H *J. Mater. Chem. C* **2013**, *1*, 8011; (d) Frizonab, T. E.; Dal-Bób, A. G.; Lopezb, G.; da Silva Paulab, M. M; da Silva, L. *Liq. Cryst.* **2014**, *41*, 1162.
123. (a) Qu, S.; Li, Y.; Wang, L.; Lu, Q.; Liu, X. *Chem. Commun.* **2011**, *47*, 4207; (b) Qu, S.; Li, M. *Tetrahedron* **2007**, *63*, 12429; (c) Qu, S.; Zhao, L.; Yu, Z.; Xiu, Z.; Zhao, C.; Zhang, P.; Long, B.; Li, M. *Langmuir* **2009**, *25*, 1713; (d) Qu, S.; Wang, L.; Liu, X.; Li, M. *Chem. Eur. J.* **2011**, *17*, 3512.
124. Han, J.; Wang, Z.-Z.; Wua, J.; Zhua, L.-R. *RSC Adv.* **2015**, *5*, 47579.
125. Zheng, C.; Yuan, A.; Zhang, Z.; Shen, H.; Bai, S.; Wang, H. *J. Fluoresc.* **2013**, *23*, 785.
126. Liu, Q.; Bian, W.; Shi, H.; Fan, L.; Shuang, S.; Dong, C.; Choi, M. M. F. *Org. Biomol. Chem.* **2013**, *11*, 503.
127. Liu, Q.; Feng, L.; Yuan, C.; Zhang, L.; Shuang, S.; Dong, C; Huc, Q.; Choi, M. M. F. *Chem. Commun.* **2014**, *50*, 2498.
128. Mashraqui, S. H.; Sundarama, S.; Bhasikuttan, A. C. *Tetrahedron* **2007**, *63*, 1680.
129. Tang, L.; Dai, X.; Zhong, K.; Wu, D.; Wen, X. *Sens. Actuators B* **2014**, *203*, 557.
130. Tang, L.; Zheng, Z.; Huang, Z.; Zhong, K.; Bian, Y.; Nandhakumar, R. *RSC Adv.* **2015**, *5*, 10505.
131. Ambrosi, G.; Formica, M.; Fusi, V.; Giorgi, L.; Macedi, E.; Micheloni, M.; Paoli, P.; Pontellini, R.; Rossi, P. *Inorg. Chem.* **2010**, *49*, 9940.
132. Li, A.-F.; Ruan, Y.-B.; Jiang, Q.-Q.; He, W.-B.; Jiang, Y.-B. *Chem. Eur. J.* **2010**, *16*, 5794.
133. Köhler, C.; Rentschler, E. *Eur. J. Inorg. Chem.* **2016**, 1955.
134. Ma, J.; Li, Z.; Zong, Y.; Men, Y.; Xing, G. *Tetrahedron Lett.* **2013**, *54*,1348.
135. Kwak, C. K.; Lee, C.-H.; Lee, T. S. *Tetrahedron Lett.* **2007**, *48*, 7788.
136. Kim, T. H.; Lee, C.-H.; Kwak, K. G.; Choi, M. S.; Park, W. H.; Lee, T. S. *Mol. Cryst. Liq. Cryst.* **2007**, *463*, 255.
137. Tang, L.; Zheng, Z.; Zhong, K.; Bian, Y. *Tetrahedron Lett.* **2016**, *57*, 1361.
138. Emmerling, F.; Orgzall, I.; Reck, G.; Schulz, B. W.; Stockhause, S.; Schulz, B. *J. Molec. Str.* **2006**, *800*, 74.
139. Huang, Z.; Song, H.-B.; Du, M.; Chen, S.-Y.; Bu, X.-H.; Ribas, J. *Inorg. Chem.* **2004**, *43*, 931.
140. Fang, Z.-L.; He, J.-G.; Zhang, Q.-S.; Zhang, Q.-K.; Wu, X.-Y.; Yu, R.-M.; Lu, C.-Z. *Inorg. Chem.* **2011**, *50*, 11403.
141. Du, M.; Li, C.-P.; You, Y.-P.; Jiang, X.-J.; Cai, H.; Wang, Q.; Guo, J-.H. *Inorg. Chim. Acta* **2007**, 2169.
142. Dong, Y.-B.; Cheng, J.-Y.; Wang, H.-Y.; Huang, R.-Q.; Tang, B.; Smith, M. D.; zur Loye, H.C. *Chem. Mater.* **2003,** *15*, 2593.
143. Atoub, N.; Mahmoudi, G.; Morsali, A. *Inorg. Chem. Commun.* **2007**, *10*, 166.

144. (a) Dong, Y.-B.; Ma, J.-P.; Huang, R.-Q.; Smith, M. D.; zur Loye, H.-C. *Inorg. Chem.* **2003**, *42*, 294; (b) Dong, Y.-B.; Cheng, J.-Y.; Huang, R.-Q.; Smith, M. D.; zur Loye, H.-C. *Inorg. Chem.* **2003**, *42*, 5699.
145. Chen, J.; Liu, S.-Y.; Li, C.-P. *Inorg. Chim. Acta* **2011**, *378*, 206.
146. Du, M.; Chen, S. T.; Bu, X. H.; Ribas, J. *Inorg. Chem. Commun.* **2006**, *5*,1003.
147. Klingele, J.; Kaase, D.; Schmucker, M.; Lan, Y.; Chastanet, G.; Létard, J.-F. *Inorg. Chem.* **2013**, *52*, 6000.
148. Dong, Y.-B.; Ma, J.-P.; Huang, R.-Q.; Smith, M. D.; zur Loye, H.-C. *Inorg. Chem.* **2003**, *42*, 294.
149. (a) Dong, Y.-B.; Wang, H.-Y.; Ma, J.-P.; Shen, D.-Z.; Huang, R.-Q. *Inorg. Chem.* **2005**, *44*, 4679; (b) Dong, Y.-B.; Xu, H.-X.; Ma, J.-P.; Huang, R.-Q. *Inorg. Chem.* **2006**, *45*, 3325.
150. Dong, Y.-B.; Zhang, Q.; Wang, L.; Ma, J.-P.; Huang, R.-Q.; Shen, D.-Z.; Chen, D.-Z. *Inorg. Chem.* **2005**, *44*, 6591.
151. Hou, S.; Liu, Q.-K.; Ma, J.-P.; Dong, Y.-B. *Inorg. Chem.* **2013**, *52*, 3225.
152. Zheng, Y.; Batsanov, A. S.; Bryce, M. R. *Inorg. Chem.* **2011**, *50*, 3354.
153. Godefroid, G.; Juanjuan, S.; Xiaochun, Q.; Yuqi, L.; Yanling, S.; Xiaohonga, S.; Zhijian, W. *Dalton Trans.* **2012**, *41*, 10228.
154. Xu, Q.-L.; Li, H.-Y.; Wang, C.-C.; Zhang, S.; Li, T.-Y.; Jing, Y.-M.; Zheng, Y.-X.; Huang, W.; Zuo, J.-L.; You, X.-Z. *Inorg. Chim. Acta* **2012**, *391*, 50.
155. Carli, S.; Correa Baena, J. P.; Marianetti, G.; Marchetti, N.; Lessi, M.; Abate, A.; Caramori, S.; Gratzel, M.; Bellina, F.; Bignozzi, C. A.; Hagfeldt, A. *ChemSusChem* **2016**, *9*, 657.
156. (a) Mane, S. B.; Cheng, C. F.; Sutanto, A. A.; Datta, A.; Dutta, A.; Hung, C.-H. *Tetrahedron*, **2015**, *71* 7977; (b) Srinivav, K; Sivakumar, G.; Ramesh Kumar, C.; Ananth Reddya, M.; Bhanuprakasha, K.; Jayathirtha Rao, V.; Chenc, C.-W.; Hsuc, Y. C.; Linc, J. T. *Synth. Metals* **2011**, *161*, 1671.
157. Wang, Z.; Zhang, H.; Killian, B. J.; Jabeen, F.; Pillai, G. G.; Berman, H. M.; Mathelier, M.; Sibble, A. J.; Yeung, J.; Zhou, W.; Steel, P. J.; Hall, C. D.; Katritzky, A. R. *Eur. J. Org. Chem.* **2015**, 5183.
158. Dacons, J. C.; Sitzmann, M. E. *J. Heterocycl. Chem.* **1977**, *14*, 1151.
159. Klapçtke, T. M; Witkowski, T. G. *ChemPlusChem* **2016**, *81*, 357.